As such, the above amendments introduce no new matter to the application and their entry by the Examiner is respectfully requested.

Attached hereto is a marked up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Claims 1-17, 53 and 60-77 were rejected under 35 U.S.C. §112, 2nd ¶ for the asserted reason that the use of the term "stably associated" in the claims renders the claim language indefinite. However, the term "stably associated" is clearly defined at page 7, lines 27 ff, which section states in part:

> By "stably associated" it is meant that the oligonucleotides of the spots maintain their position relative to the solid support under hybridization and washing conditions. As such, the oligonucleotide members which make up the spots can be non-covalently or covalently stably associated with the support surface based on technologies well know to those of skill in the art.

As such, the term "stably associated," when read in light of the specification by one of skill in the art, is not indefinite as one of skill in the art would clearly know what is meant by this term. Therefore, the Examiner is respectfully requested to withdraw this rejection.

In the Office Action, Claims 1, 2, 5-10, 12-17, and 57-58 were rejected under 35 U.S.C. § 102 as being anticipated by Brown et al (U.S. Pat. No. 5,807,522). During the above referenced interview, the Examiner explained that this rejection was maintained because the Examiner did not see how the claim language distinguished over Brown.

In view of the above amendments, the Applicants submit that the claims clearly distinguish over the Brown disclosure. In the present claims, the two or more different probes of the arrays hybridize to the same target nucleic acid to produce a complex that is made up

of the two or more probes and the target nucleic acid. The following figure further illustrates this feature:

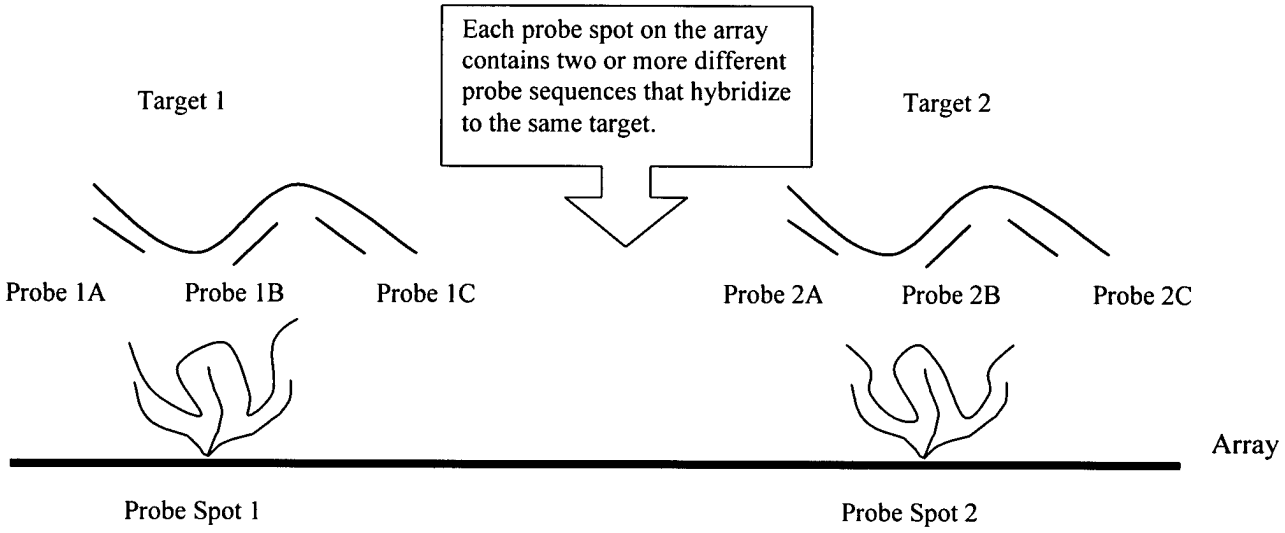

Figure 1. Probe spot 1 contains probes 1A, 1B and 1C;
Probe spot 2 contain probes 2A, 2B and 2C in the array shown above.

As shown in the above figure, each probe spot is designed so that upon hybridization of the target to its probe spot, a complex is formed with the target and the two or more different probes of the probe spot.

In contrast, Brown does not teach such an array. In the cell of different regions cited by the Examiner as anticipatory of the probe spots of the present array, the probe nucleic acids are not close enough to each other to provide for the complexes of target and two or more probes, as required in the claimed arrays. Furthermore, where one views each region of the Brown array as a mixture of two or more probes because of the manner in which the probes are produced, i.e., by PCR which produces a mixture of probes, the probes will **not** produce complexes with the target as required by the claim because each probe will hybridize

to only a single target and will not hybridize to a target that is already hybridized to another probe.

As such, Brown does not meet each and every limitation of the claimed invention because Brown fails to teach or suggest an array in which the probes of each spot are selected to produce a complex of a single target molecule and two or more probes. Accordingly, Claims 1, 2, 5-10, 12-17, and 57-58 are not anticipated under 35 U.S.C. § 102 over Brown and this rejection may be withdrawn.

Claims 1-3, 5-8, 13-17, 53 and 59 were rejected under 35 U.S.C. § 102 over Pinkel for the asserted reason that Example 1 teaches an array that anticipates these claims.

However, Example 1 actually prepares two collections of nucleic acid coated particles, not an array. Furthermore, the nucleic acids on the particles range in length from several hundred basepairs to over 10 kb. These nucleic acids are double-stranded because described in terms of bp and they are not oligonucleotides. As such, Example 1 fails to anticipate the claimed invention.

More importantly, however, nothing in Pinkel teaches or suggests the claimed invention as now claimed, in which the oligonucleotide probes of each spot form a complex with the same target nucleic acid, as described above.

As such, Pinkel fails to anticipate the invention of Claims 1-3, 5-8, 13-17, 53 and 59, and this rejection may be withdrawn.

Claims 3-4 were rejected under 35 U.S.C. § 103(a) over Brown et al in view of Fodor et al. (U.S. Pat. No. 5,800,992, filed June 25, 1996) for the asserted reason that Brown teaches all of the limitations of the claimed invention except for the placement of the probes on the array corresponding to non-overlapping or overlapping regions of a target nucleic acid, which is assertedly supplemented by the Fodor et al. reference.

However, as indicated above, Brown is fundamentally deficient in failing to teach or suggest an array having a probe spot where the oligonucleotide probes form a complex with the target nucleic acid such that the complex is made up of at least two different oligonucleotide probes hybridized to the same target nucleic acid.

Fodor fails to make up this fundamental deficiency in the Brown reference. Fodor teaches that "probes of known . . . sequence may be immobilized to the matrix and a map of **various different target sequences** may be determined from overlaps." (Col. 10, lines 9-12). Thus, Fodor suggests using probes to map or determine the sequential ordering of a plurality of various sequences using probes that hybridize to various different target sequences. In other words, different probe spots on the Fodor array may include probes that hybridize to different regions of the same target nucleic acid sequence. **However, each probe spot on the Fodor array is made up of identical probes, not two or more different probes of different sequence. Furthermore, nowhere does Fodor suggest that the probes in each spot hybridize to the same target to produce a complex, as required in the claims of the present application.** As such, Fodor fails to make up the fundamental deficiency in the Brown teaching.

As such, the combined teachings of the cited references fail to teach or suggest an array of probe oligonucleotide spots where each spot contains a plurality of unique oligonucleotides of different sequence that each hybridize to the same target nucleic acid to produce a complex of the target nucleic acid and the two or more probes. Because this element of the claimed invention is neither taught nor suggested by the combined teachings of the cited references, Claims 3-4 are not obvious under 35 U.S.C. § 103(a) over Brown in view of Fodor and this rejection may be withdrawn.

Claim 11 was rejected under 35 U.S.C. §103(a) over Brown in view of a Lockhart et. al. (U.S. Pat. No. 6,040,138, filed June 7, 1995) for the asserted reason that Brown teaches the array of the present invention but for the element of at least one mismatch probe on the array, which this missing element is provided by the Lockhart reference. However, as demonstrated above, the Brown reference fails to teach or suggest the fundamental element

that each probe spot be made up solely of a mixture of at least two different oligonucleotides of different sequence that hybridize to the same target nucleic acid to produce a complex of the target nucleic acid and the two or more oligonucleotide probes. As Lockhart is cited solely for his teaching of mismatch probes, this reference fails to make up this fundamental deficiency of Brown. Accordingly, Claim 11 is not obvious over Brown in view of Lockhart and this rejection may be withdrawn.

Claims 53 and 59 have been rejected under 35 U.S.C. §103(a) over Brown et al. in view of a Stratagene catalog (1988), page 39 for the asserted reason that Brown teaches arrays of the claimed invention (i.e. the array according to Claim 1) but for the motivation to combine reagents with the array to make up the kit, which missing element is provided by the Stratagene reference. However, as demonstrated above, the Brown reference fails to teach or suggest the fundamental element that each probe spot contain at least two different oligonucleotides of different sequence that hybridize to the same target nucleic acid to produce a complex of the target nucleic acid and the at least two different oligonucleotide probes. As the Stratagene reference is cited solely for the teaching of kits in general, this reference fails to make up this fundamental deficiency of Brown. Accordingly, Claims 53 and 59 are not obvious over Brown in view of Stratagene and this rejection may be withdrawn.

Claims 4, 9-10, 12, 57 & 58 have been rejected under 35 U.S.C. §103(a) over Pinkel. However, as demonstrated above, the Pinkel reference fails to teach or suggest the fundamental element that each probe spot contain at least two different oligonucleotides of different sequence that hybridize to the same target nucleic acid to produce a complex of the target nucleic acid and the at least two different oligonucleotide probes. Accordingly, Claims 5, 9-10, 12, 57 & 58 are not obvious over Pinkel and this rejection may be withdrawn.

Claims 11 and 70 were rejected under 35 U.S.C. §103(a) over Pinkel in view of a Lockhart et. al. (U.S. Pat. No. 6,040,138, filed June 7, 1995) for the asserted reason that Pinkel teaches the array of the present invention but for the element of at least one mismatch probe on the array, which missing element is provided by the Lockhart reference. However,

as demonstrated above, the Pinkel reference fails to teach or suggest the fundamental claimed element that each probe spot be made up solely of a mixture of at least two different oligonucleotides of different sequence that hybridize to the same target nucleic acid to produce a complex of the target nucleic acid and the two or more oligonucleotide probes. As Lockhart is cited solely for his teaching of mismatch probes, this reference fails to make up this fundamental deficiency of Pinkel. Accordingly, Claims 11 and 70 are not obvious over Pinkel in view of Lockhart and this rejection may be withdrawn.

Claims 60-69 and 71-76 were rejected under 35 U.S.C. §103(a) over Pinkel in view of Lapidus. As demonstrated above, the Pinkel reference fails to teach or suggest the fundamental element of the claims that each probe spot be made up solely of a mixture of at least two different oligonucleotides of different sequence that hybridize to the same target nucleic acid to produce a complex of the target nucleic acid and the two or more oligonucleotide probes. Lapidus also fails to teach or suggest such a probe spot and therefore fails to make up this deficiency in the primary Pinkel reference. Accordingly, Claims 60-69 and 71-76 are not obvious over Pinkel in view of Lapidus and this rejection may be withdrawn.

Claims 1-8 and 14-17 were rejected under the judicially created doctrine of obviousness type double patenting over Claims 1-17 of U.S. Patent No. 6,077,673 for the asserted reason that Claims –18 and 14-17 are generic with respect to these previously issued claims. In view of the above amendments and clarification of the claim invention of these claims, the Examiner is respectfully requested to reconsider this position as it is unclear to the undersigned how the present claims are generic to Claims 1-17 of 6,077,673, since the claims of the present application require that two or more probes of a spot hybridize to the same target to produce a complex with it and the claims of the cited patent encompass the structure where the probes do not form such a complex with a target, i.e., each probe hybridizes to only a single target.

Claim 10 was provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of Claim 1 of copending application serial no. 09/440,829. Claim 1 of this copending application reads as follows:

> 1. An array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe oligonucleotide spot of said pattern corresponds to a target nucleic acid and comprises an oligonucleotide probe composition made up of long oligonucleotide probes that range in length from about 50 to 120 nt.

Claim 10 of the present application reads as follows:

> 10. The array according to Claim 1, wherein each of said oligonucleotides ranges from about 15 to 150 nucleotides in length.

Since the array of Claim 10 is dependent on Claim 1, it includes the element that two or more probes hybridize to the same target to produce a complex. This element is not present in Claim 1 of the cited copending application and therefore the two claims are not claiming the same invention. The Examiner is therefore respectfully requested to withdraw this rejection.

Finally, Claims 1-17 and 53 were provisionally rejected under the judicially created doctrine of obviousness type double patenting over Claims 1-23 and 35 of copending application serial no. 09/440,829. In view of the above amendments and discussion regarding the present claims, the Applicants respectfully submit that Claims 1-17 and 53 are patentably distinct from these claims of the copending application. As such, the Examiner is respectfully requested to reconsider this rejection in view of the above amendments and withdraw this rejection.

In view of the attached amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,

BOZICEVIC, FIELD & FRANCIS LLP

Date: 5·23·01

By: _____
Bret Field
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encs:

- Marked up Copy of Amended Claims
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) An array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridize to the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides.

57. (Amended) An array comprising a pattern of probe oligonucleotide spots, wherein each probe oligonucleotide spot comprises an oligonucleotide probe composition consisting of a mixture of 3 to 50 unique oligonucleotides of different sequence and from about 15 to 150 nucleotides in length that hybridize to a different region of the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides. ~~, wherein each unique oligonucleotide hybridizes to a different region of said target nucleic acid of the probe oligonucleotide spot~~.

58. (Amended) An array comprising a pattern of probe oligonucleotide spots of a density that does not exceed about 400 spots/cm^2, wherein each probe oligonucleotide spot consists of a mixture of 3 to 20 unique oligonucleotides of different sequence and from about 25 to 100 nucleotides in length that hybridize to a different region of the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides. ~~, wherein each unique oligonucleotide hybridizes to a different region of the said target nucleic acid.~~

60. (Amended) An array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that cooperatively hybridize to the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides.